EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 6
Issue: 6
200-202
Year: 2019

SYNTHESIS OF RECENT DERIVATIVES OF ANTIHYPERTENSIVE DRUGS

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Article Received on 08/04/2019 **Article Revised on 29/04/2019** **Article Accepted on 20/05/2019**

ABSTRACT
The present review work focuses on the synthesis of various derivatives of antihypertensive drugs. Hypertension, the most common cardiovascular risk factor needs to be focussed in the present era. The increase in blood pressure is the major cause for the variety of leading dysfunction of body in the individuals. The synthesis of various derivatives of antihypertensive agents have been discussed which will surely help in the decrease in this cardiovascular disease called hypertension.

KEYWORDS: Hypertension, synthesis, antihypertensive drugs, cardiovascular disease.

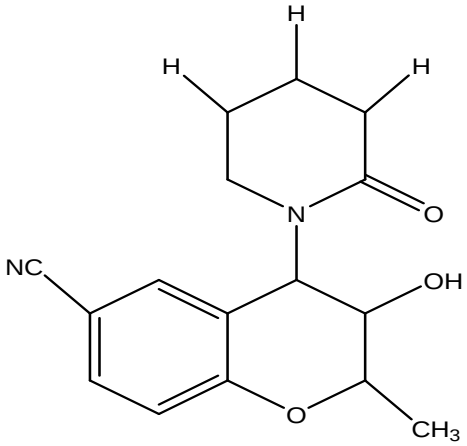
INTRODUCTION

Hypertension is the cardiovascular disease and it is the most common modifiable risk factor and may some time it cause death. The increased risk associated with blood pressure can be reduced by the treatment with antihypertensive drugs.[1] Antihypertensive drugs lower both BP and related target organ damage. The principal effector of aldosterone action is the mineralocorticoid receptor (MR), a nuclear transcription factor that is expressed at high levels in the cortical collecting duct of the kidney.[2]

It is the second leading cause of chronic kidney disease (CKD). More than one billion adults are hypertensive worldwide and this figure is projected to increase to 1.56 billion by the year 2025, which is an increase of 60% from 2000 is estimated.[3] In the hypertension patients clinical evidence suggests that lowering blood pressure (BP) with antihypertensive drugs reduces the risk of myocardial infarction, stroke, heart failure, revascularization procedures and end-stage renal diseases.[4] Every year 9.4 million death occur worldwide because of hypertension[5], with it being responsible for about 50% of mortality due to heart disease and stroke.[6] The various behavioural risk factors, such as unhealthy diet, excess use of alcohol, sedentary lifestyle, obesity, and exposure to persistent stress increase the chance of hypertension. Epidemiological studies demonstrated that prevalence of hypertension is increasing rapidly in India, it is varying from 4 to 15% in urban and 2-8% in rural population.[7,8] The numerous antihypertensive drugs are available to cure this chronic disease.[9]

REVIEW

1. **Synthesis and Antihypertensive Activity of 4-(1,2-Dihydro-2-oxo-1-pyridyl)-2H-1-benzopyrans and Related Compounds, New Potassium Channel Activators.** The synthesis and antihypertensive activity of 4-(1,2-Dihydro-2-oxo-1-pyridyl)-2H-1-benzopyran-3-ols are described. The compound 7e is highly active, with substituents on the pyridine ring leading to a decrease in activity. The elimination of water from the chromanols leads to the formation of the chromenes, which are among the most potent antihypertensive known. The compounds **1, 2** and **3** are highly active and showed antihypertensive activity.[10]



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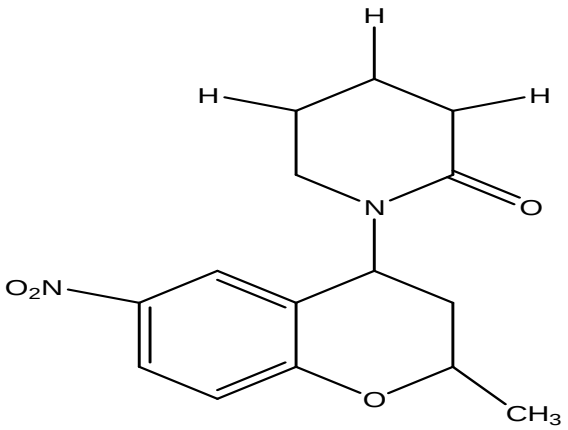

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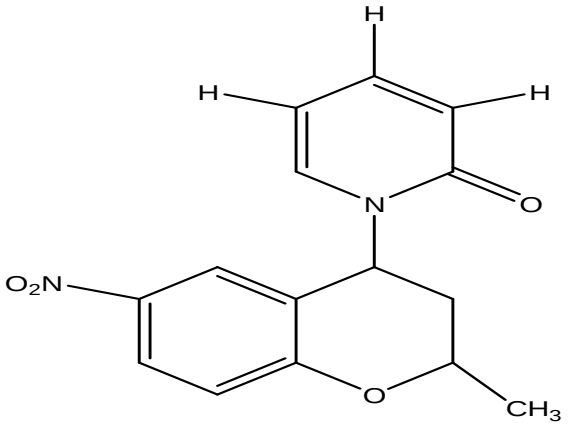

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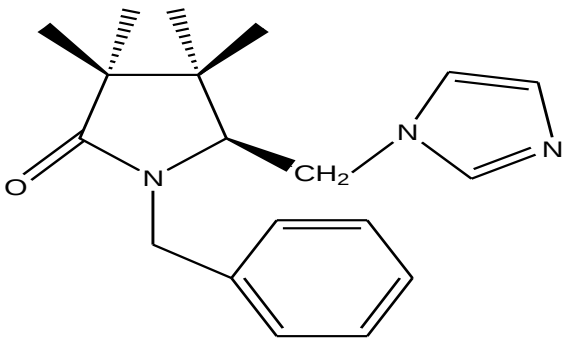
2. **Design and Synthesis of Novel Antihypertensive Drugs.** For the treatment of hypertension, a new generation of drugs that is AT1 antagonists were design and synthesis. They have the ability to mimic the C-terminal segment of angiotension II. The binding action is blocked on AT1 receptor such a compound is synthesised **4**. It may serve as a new antihypertensive molecule.[11]



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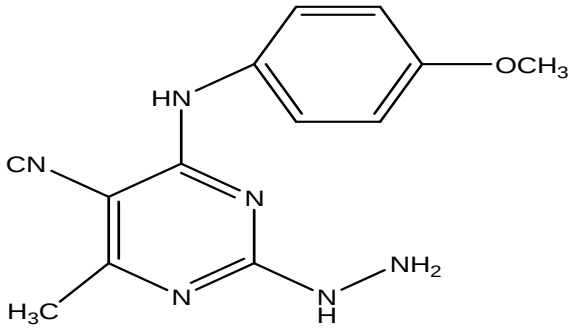
3. **Design, synthesis and antihypertensive activity of new pyrimidine.** Pyrimidine derivatives based on nifidipine-like structure was designed and synthesized. We are found to exhibit calcium channel blocker and preparation of rabbit aorta. The range in the exhibit relaxation 89.2%, 74.4% in comparison to nifidipine to decrease heart rate. Histopathological effect of compound **5, 6, 7** on the expression endothelial nitric oxide was examined on aorta.[12]



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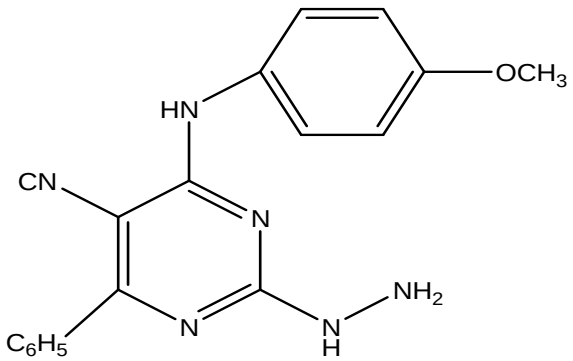

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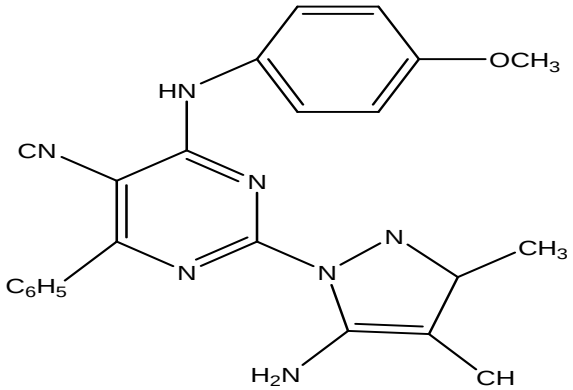

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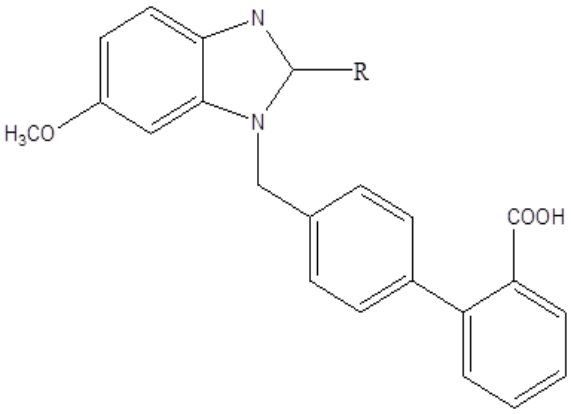
4. **Synthesis and antihypertensive activity of some new benzimidazole derivatives of 4'-(6-methoxy-2-substituted-benzimidazole-1-ylmethyl) biphenyl-2-carboxylic acid in the presences of BF3·OEt2.** A series of 4,6-methoxy to substitutes benzimidazole, 1 methyl by phenyl carboxyl acid

were synthesised by 4-methxy-1,2-phenylamine and difference substituted carboxylic acid in the presence of BF3 as a catalyst with biphenyl carboxylic acid and forms the compound **8.**[13]



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CONCLUSION

The present review focuses on the discussion of hypertension, its pathophysiology, antihypertensive drugs and basically on the synthesis of various derivatives which can be further modified from the present antihypertensive drugs. Some of the synthesis discussed involves 4-(1,2-Dihydro-2-oxo-1-pyridyl)-2H-1-benzopyrans and Related Compounds; benzimidazole derivatives of 4'-(6-methoxy-2-substituted-benzimidazole-1-ylmethyl) biphenyl-2-carboxylic acid; etc. The work will definitely help in providing the knowledge about hypertension and various drugs that can be further synthesised for its treatment.

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